REMARKS

Claims 2-25 are in this application. Claim 6 has been amended to correct a typographical error. Support for the amendment is found on page 4, line 19 of the specification.

The Examiner has rejected claims 2-21 and 25 under 35 USC 102(a) as being anticipated by Sachs (US Patent 5,945,124). The Examiner has rejected claims 2-21 and 25 under 35 USC 102(e) as being anticipated by Sachs (US Patent 5,945,124 or US Patent 6,086,856). Applicants respectfully traverse these rejections.

U.S. Patents 5,945,124 and U.S. 6,068,856 (Sachs) disclose oral pharmaceutical compositions of pantoprazole in pellet form which contain (see columns 4-5 and example 3):

a) an alkaline nucleus;
b) a layer containing pantoprazole, HMPC (polymer soluble in water), propylene glycol and NaOH;
c) a release-slowing layer containing ethylcellulose (polymer insoluble in water) and HMPC (polymer soluble in water); and,
d) an outer enteric coating.

See column 4, lines 51-54 and column 5, lines 21-23 of U.S. Patent 6,068,856.

The starter and active pellets of example 3 are made using NaOH.

Claim 25 of this application defines:

A pellet comprising an acid labile benzimidazole compound, wherein the pellet comprises:

(a) an inert nucleus;

(b) a layer disposed over said inert nucleus (a), consisting of an acid labile benzimidazole compound, an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients;

(c) one or more intermediate layers that comprise:

(i) an inert, non-alkaline coating, formed of an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients; and

(ii) a system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert polymer insoluble in water; said intermediate layer(s) (c) disposed over said layer (b) that covers the inert nucleus; and

(d) an external layer comprising an enteric coating disposed over said intermediate layer(s) (c).

According to the Examiner (see page 5, item 9 of the Office Action), the argument put forward by the applicants that layer (b) which consists of an acid labile benzimidazole compound, an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients should overcome the prior art since the sodium hydroxide of the prior art is not required by the present invention, is not found persuasive. The justification indicated by the Examiner is that section (b) includes one or more pharmaceutically acceptable inert excipients and sodium hydroxide is within this limitation, since the specification defines "inert" as not reacting with the active ingredient.

It is accepted that the specification states (see page 6, lines 32-34) "*In the sense used in this specification the term "inert", applied to a polymer of an excipient, refers to the fact that said compounds do not react in the conditions used*". However, it has also to be accepted that if NaOH (or any other alkaline excipient) is present in layer (b) of the pellet of the invention it will actually react with the acid labile benzimidazole compound to form the sodium salt of said benzimidazole. Consequently, since NaOH would react in the conditions used, NaOH (or any other alkaline excipient) cannot be included in the definition of layer (b) of claim 25.

The Examiner argues further that column 4, lines 20-31 of U.S. Patent 5,945,124, teaches the omission of the sodium hydroxide in the intermediate layer since said passage of the patent document states that the sodium hydroxide is added only to increase the buffering capacity if this is so desired. Accordingly, the

Examiner maintains the rejection of the patent, since the absence of any alkaline excipient in layer (b) of the invention would not confer novelty.

The Applicant cannot agree with this reasoning of the Examiner since lines 20-31 in column 4 of U.S. Patent 5,945,124 refer to what we have called layer c) of the composition, but not to layer b). Actually, according to lines 3-6 of column 4 of U.S. Patent 5,945,124, pantoprazole is present either in the form of its alkaline salts or together with alkaline substances (this would correspond to layer b).

In fact the text at col. 4, lines 20-24 is "The intermediate layer or intermediate layers act as pH-buffering zones in which hydrogen ions, which diffuse in from the outside, are able to react with the hydroxyl ions which diffuse out of the alkaline core (emphasis added).

Consequently, whereas the U.S. Patent 5,945,124 teaches that layer b) contains pantoprazole either in the form of its alkaline salts or together with alkaline substances, and that layer c) may include alkaline substances; claim 25 of the present application defines a composition in which layer (b) does not contain alkaline compounds and in which the benzimidazole compound in layer (b) is not in the form of its alkaline salt (acid labile bencimidazole). Furthermore, layer (c) of the present invention does not contain any alkaline compound either.

Accordingly, Claims 2-25 are novel and it is respectfully requested that the rejection be withdrawn.

The Examiner has rejected claims 2-21 and 25 as being obvious under 35 USC 103 in view of U.S. Patents 5,945,124 and 6,068,856.

Applicants respectfully traverse this rejection.

U.S. Patent 5,945,124 and U.S. Patent 6,068,856 disclose pellets of modified release of pantoprazole (an acid labile benzimidazole compound) in which the problem related to the stability of the active compound (benzimidazole) is solved by using alkaline salts of the pantoprazole and/or incorporating a compound of alkaline reaction (NaOH). According to col. 4, lines 3-6 of the '856 patent , "In the case of pantoprazole, which in [sic] very acid-labile, it is necessary to process it in the tablet core or in pellets in the form of its alkaline salts, for

example, as sodium salts, or together with alkaline substances." The present invention is pellets of modified release of acid labile benzimidazole compounds in which the problem related to the stability of the benzimidazole is solved in a different way. In applicants' composition there is no alkaline compound in the layer b). Given the disclosure in the '856 patent and in the '124 patent that it is a requirement to process the acid labile compound in the form of its alkaline salts or together with alkaline substances, it is not obvious that a system of modified release of an acid labile benzimidazole compound can be prepared where the benzimidazole compound is not in the form of an alkaline salt or is together with an alkaline substance.

The Applicant has surprisingly found that when employing at least one intermediate layer c) that comprise i) one or more non alkaline inert coating and ii) one or more layers that contain a system of modified release, it is no longer necessary for achieving stability of the acid labile benzimidazole (active ingredient) that such compound be in the form of an alkaline salt and/or be together with compounds of alkaline reaction.

The standard test used to establish *prima facie* obviousness is the test set out by the Supreme Court in **Graham v. John Deere** (383 US 1, 148 USPQ 459 (1966)). To determine whether a claim is *prima facie* obvious:

1) the scope and content of the prior art are to be determined;
2) the differences between the prior art and the claims at issue are to be ascertained; and
3) the level of ordinary skill in the pertinent art resolved.

In addition, according to MPEP 2141, citing **Hodosh v. Block Drug Co., Inc.**, 86 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n. 5 (Fed. Cir. 1986), when applying 35 USC 103, the following tenets of patent law must be adhered to:

1) the claimed invention must be considered as a whole;
2) the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
3) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and
4) reasonable expectation of success is the standard with which

obviousness is determined.

The references do not suggest the desirability of preparing a system of modified release for an acid labile benzimidazole compound that does not contain an alkaline salt of the benzimidazole compound or the benzimidazole in an alkaline environment. In fact, the references teach away from what applicants have done because the references teach that the pantoprazole must be in the form of an alkaline salt or in an alkaline environment. Therefore, there is no reasonable expectation of success based on the cited references.

Therefore, the invention of claims 2-21 and 25 is not obvious, and it is respectfully requested that the rejection be withdrawn.

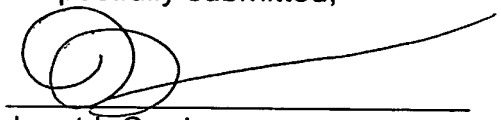
The Examiner has rejected claims 22-25 as being obvious over U.S. Patent 5,945,124 in view of Paradissis (U.S. Patent 5,445,829) or U.S. Patent 6,068,856 in view of Paradissis (U.S. Patent 5,445,829). Applicants respectfully traverse this rejection.

Claims 22-25 depend directly or indirectly from claim 25. Since claim 25 is not obvious claims 22-25 are not obvious.

Therefore, it is respectfully requested that this rejection be withdrawn.

Applicants submit that the instant invention is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,



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